STAT3, these results could not be observed. In vivo results demonstrated that after surgery of hindlimb ischemia, mice (n=12) treated with JI-34 pretreated MSC, MSC and PBS revealed a significantly difference of limb recovery and rebuildment of newly formed vessels. Ultrasound Doppler displayed that mice injected with treated cells gained a better recovery of blood perfusion in day 3 after surgery and sustained to day14 than MSC and PBS group. Immunofluorescence of CD31, a-SMA, TUNEL and immunohistochemistry also supported the results that treated with JI-34, MSC increased vascularation and angiogenesis of mice hindlimb ischemia.
Conclusions: the agonist of GHRH can activate the receptor of MSC to enhance its viability and paracrine effect through STAT3 signaling pathway to promote the angiogenesis of ischemic hindlimb of mice.

GW25-e3569

Targeted Delivery of Hydrogen Sulfide Using Ultrasound and Intravenous Microbubbles Attenuates Myocardial Ischemia-reperfusion Injury

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Objectives: Myocardial ischemia-reperfusion injury is a major cause of cardiac damage following revascularization in acute myocardial infarction. Hydrogen Sulfide (H_2S) has emerged as a critical signaling molecule with a profound cardioprotective effect. However, systemic delivery of H_2S is hampered by cytotoxicity. We hypothesized that intravenous administration of microbubbles encapsulating H_2S gas combined with ultrasound exposure permit safe and local release of H_2S and attenuate myocardial ischemic-reperfusion injury.
Methods: A 1:1 mixture of the H_2S (4ml) and perfluorocarbons (4ml) was encapsulated into microbubbles (H_2S-MB), while microbubbles containing 8ml of perfluorocarbons (PESDA) served as control. Wistar rats were subjected to temporary ligation of the left coronary artery for 45min. H_2S-MB or PESDA were administered intravenously 5min prior to reperfusion for 10min with or without ultrasound applied over the heart. H_2S concentrations were measured in plasma and tissue homogenate (heart, lung, kidney and brain) by methylene blue assay. Infarct size was determined by evans blue and TTC staining. Serum levels of the cardiac-specific isoform of troponin-I (cTnI) were assessed 4h after reperfusion. Left ventricular structure and function was assessed by echocardiography 3 weeks after reperfusion.
Results: Intravenous H_2S-MB administration in combination with the ultrasound exposure enhanced the concentrations of H_2S in the myocardial and lung tissue ($P<0.05$). Rats receiving H_2S-MB and ultrasound representing a significant reduction in infarct size and serum levels of cTnI as compared with PESDA and ultrasound treated rats (28.0±2.6% vs 44.6±4.5%, P=0.005; 7.6±1.5 ng/ml vs 13.3±2.0 ng/ml, P=0.019, respectively). There were significant differences in ejection fraction between H_2S-MB group and PESDA group both treated with ultrasound exposure (48.6±1.5% vs 41.0±2.0%, P=0.006). No significant hemodynamic differences between H_2S-MB and PESDA were observed.
Conclusions: Targeted delivery of H_2S using ultrasound and intravenous microbubbles limits the extent of myocardial ischemia-reperfusion injury. This may provide a noninvasive strategy for targeted delivery of a therapeutic gas to protect myocardial injury from ischemia–reperfusion, avoiding systemic side effects.

GW25-e4138

Vasomotor effect of salidroside on rat mesenteric artery and its regulatory mechanisms

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Objectives: To observe vasomotor effect of salidroside (SAL) on rat mesenteric artery, and to explore its underlying regulatory mechanisms.
Methods: Tension was measured by DMT 610M system to evaluate the vasomotor effect of SAL on rat endothelium-intact and endothelium-denuded mesenteric artery rings. L-NAME, an inhibitor of nitric oxide synthase (NOS), indomethacin, a Cyclooxygenase (COX) inhibitor, calcium deprivation and calcium addition were used to illustrate the mechanisms of vasomotor effect of SAL.
Results: SAL (10^{-8}mol/L - 10^{-4} mol/L) neither had significant effect on mesenteric artery rings keeping the basic state nor ones precontracted by KCl (6×10^{-2}mol/L) ($P>0.05$). SAL relaxed endothelium-intact and endothelium-denuded mesenteric artery precontracted by phenylephrine (2×10^{-6}mol/L) in concentration-dependent manner, while the vasodilation of endothelium-intact mesenteric artery was significantly stronger than that of endothelium-denuded one ($P<0.01$ in 10^{-5} mol/L SAL and $P<0.001$ in 10^{-4} mol/L SAL). Pretreatment with L-NAME (10^{-4}mol/L), for 30min significantly attenuated the vasodilation of endothelium-intact mesenteric artery induced by SAL ($P<0.01$ in 10^{-5}mol/L SAL), while pretreatment with indomethacin (10^{-4}mol/L), for 30 min had no effect on the vasodilation of endothelium-intact mesenteric artery induced by SAL ($P>0.05$). With calcium deprivation and calcium addition, SAL relaxed endothelium-denuded mesenteric artery precontracted by phenylephrine (2×10^{-6}mol/L) ($P<0.01$ in 10^{-5} mol/L SAL), while SAL had no effect on the increasing tension of mesenteric artery induced by adding $CaCl_2$ ($P>0.05$).
Conclusions: These results indicate that SAL has endothelium-dependent relaxation effect on rat mesenteric artery, which might be related to the endothelial nitric oxide (NO) pathway and inhibiting release of intracelluar calcium of rat mesenteric artery. However, this vasodilation effect of SAL is not associated with voltage-dependent calcium channel, the COX pathway and influx of extracellular calcium.

GW25-e4247

Change and trend of the reperfusion injury salvage kinase and mitochondrial permeability transition pore after ischemic postconditioning in myocardial ischemia-reperfusion in rats

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Objectives: To explore the dynamic variance of the reperfusion injury salvage kinase and mitochondrial permeability transition pore after ischemic postconditioning in myocardial ischemia-reperfusionon in rats.
Methods: Lewis rats were randomly assigned to a ischemia-reperfusion or ischemic postconditioning or sham operation protocol. All groups except sham operation group underwent myocardial ischemia obtained by ligating anterior descending (LAD) branch for 30min, and followed by 3, 6, 12, 24-hour and 2, 4, 7-day reperfusion respectively.In ischemic postconditioning group, three cycles of 10s reperfusion followed by 10s LAD re-occlusion were applied during the first min of reperfusion. the expression of P-AKT and P-ERK1/2 protein were mearsured by western blot, and Spectrophotometer was used to determined the opening of mPTP at the end of the reperfusion respectively.
Results: Compared with sham operation group, the expression of P-AKT and P-ERK1/2 protein and the opening of mPTP increased ($P<0.01$) in both ischemia-reperfusion group and ischemic postconditioning group at 3, 6, 12, 24-hour and 2, 4, 7-day reperfusion. Compared with ischemia-reperfusion group, the expression of P-AKT and P-ERK1/2 protein increased ($P<0.05$), the opening of mPTP decreased ($P<0.05$) in ischemic postconditioning group. In both ischemia-reperfusion group and ischemic postconditioning group, no change in the trend of the expression of P-AKT and P-ERK1/2 protein and the opening of mPTP, and the peak-time of expression of P-AKT and P-ERK1/2 protein and the trough-time of opening of mPTP happened at 24h reperfusion.
Conclusions: Ischemic postconditioning increases the expression of P-AKT and P-ERK1/2 protein, decreases the opening of mPTP between 3 hours and 7 days after the reperfusion followed myocardial ischemia in rats. However, ischemic postconditioning does not change the trend in the expression of P-AKT and P-ERK1/2 protein and the opening of mPTP in ischemia-reperfusionon rats.

GW25-e4591

Electrophysiological study of the mechanism of action of the Traditional Chinese Medicine compound TMYX on the spontaneous activity of cardiac pacemaker cells

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Objectives: Traditional Chinese Medicine (TCM) is one of the oldest organized healing systems in the human history. The TCM approach to the disease differs from that of western medicine since it is based on the holistic view of both the diseased state and the associated therapy; modern western medicine focusses instead on the identification and treatment of specific molecular causes. Both approaches have a long history of proven results. We therefore started a collaborative project to investigate the molecular effects of a TCM drug (Tong Mai Yang Xin, TMYX, Le Ren Tang, China) which is indicated in the treatment of brady- and tachy-arrhythmias. The specific aim was to investigate whether this drug acts on the sinoatrial node (SAN).
Methods: Experiments were carried out in cells isolated from rabbit SAN. The whole-cell patch-clamp technique was used to record the spontaneous activity of SAN myocytes in the absence and in the presence of TMYX. Based on the in-vitro toxicity MTT test carried out on a cardiac cell line (H9C2) and on pilot electrophysiological experiments, we chose to investigate the action of the drug in the concentration range 0.02-2 mg/ml. The drug was dissolved in dimethyl sulfoxide (DMSO) and therefore an appropriate amount of DMSO was also added to the control solution. Action Potentials (AP) were acquired from regularly beating single cells or cell-aggregates and analyzed by a customized software. Group comparisons were carried out by paired t-test statistic (statistical significance at $P<0.05$).
Results: Stable spontaneous APs were recorded from SAN cells/aggregates before and during perfusion of TMYX. The parameters that describe the properties of each AP cycle were the following: 1) AP Rate, Maximum Diastolic Potential (MDP), Early Diastolic Depolarization (EDD), Take-Off Potential (TOP), AP Duration at 50% of repolarization (APD50). Specific details are provided in (1).

When SAN cells were challenged with 3 different concentrations (0.02, 0.2, and 0.6 mg/ml) of TMYX we observed in all cases a significant ($P<0.05$) dose-dependent